

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Susan L. Weston et al.

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Assistant Commissioner for Patents  
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**MARK-UP OF CLAIMS**  
**IN ACCORDANCE WITH 37 CFR 1.121**

**IN THE CLAIMS:**

Please amend Claims 1, 2, 3, 5, 14, 15, 16 and 17 as follows:

1. (Amended) A method for detecting the presence or absence of twelve mutations in the cystic fibrosis transmembrane conductor regulator (CFTR) gene, which method comprises contacting sample genomic DNA from an individual in two separate reaction vessels with allele specific primer sets, wherein:

A) genomic DNA in the first reaction vessel is contacted with allele specific primer sets for the 1717-1 G>A, G542X, W1282X, N1303K, ΔF508(M), 3849+10kb C>T mutations, comprising SEQ. ID. No. 5, SEQ. ID. No. 7, SEQ. ID. No. 8, SEQ. ID. No. 10, SEQ. ID. No. 12, and SEQ. ID. No. 14,  
and

- B) genomic DNA in the second reaction vessel is contacted with allele specific primer sets for the 621+1 G>T, R553X, G551D, R117H, R1162X and R334W mutations, comprising SEQ. ID. No. 16, SEQ. ID. No. 18, SEQ. ID. No. 19, SEQ. ID. No. 21, SEQ. ID. No. 23, SEQ. ID. No. 24, and SEQ. ID. No. 26,

in the presence of appropriate nucleotide-triphosphates and an agent for polymerization, such that each [diagnostic] allele specific primer is extended only when the relevant mutation is present in the sample; and detecting the presence or absence of CFTR gene alleles by reference to the presence or absence of [diagnostic] primer extension product(s).

2. (Amended) A method [as claimed in] according to claim 1, [and] wherein the sample genomic DNA is amplified using amplification primers selected from the group consisting of SEQ. ID. No. 6, SEQ. ID. No. 9, SEQ. ID. No. 11, SEQ. ID. No. 13, SEQ. ID. No. 15, SEQ. ID. No. 17, SEQ. ID. No. 20, SEQ. ID. No. 22, SEQ. ID. No. 25, and SEQ. ID. No. 27 [one or more diagnostic primers is used with one or more amplification primers in one or more cycles of PCR amplification].
3. (Amended) A set of allele specific primers for each of the following alleles of the CFTR gene mutations: 1717-1 G>A, G542X, W1282X, N1303K,  $\Delta$ F508(M), and 3849+10kb C>T, the set of allele specific primers comprising SEQ. ID. No. 5, SEQ. ID. No. 7, SEQ. ID. No. 8, SEQ. ID. No. 10, SEQ. ID. No. 12, and SEQ. ID. No. 14.
5. (Amended) A set of allele specific primers for each of the following alleles of the CFTR gene mutations: 621+1 G>T, R553X, G551 D, R117H, R1162X and R334W, comprising SEQ. ID. No. 16, SEQ. ID. No. 18, SEQ. ID. No. 19, SEQ. ID. No. 21, SEQ. ID. No. 23, SEQ. ID. No. 24, and SEQ. ID. No. 26.

14. (Amended) A set of primers comprising the following [diagnostic] allele specific primer and amplification primer sequences:

TCTTGGGATT CAATAACTTT GCAACAGTCA (Seq. ID No. 5)  
GAATTCCTCAA ACTTTTAGAG ACATC (Seq. ID. No. 6)  
TACTAMAGT GACTCTCTM TTTTCTATTT TTGGTAATTA (Seq. ID No. 7)  
AGTTTGCAGA GAAAGACAAT ATAGTTCTCT (Seq. ID. No. 8)  
TAATCTCTAC CAAATCTGGA TACTATACC (Seq. ID. No. 9)  
TGATCACTCC ACTGTTTCATA GGGATCCATC (Seq. ID. No. 10)  
AATTTGAGAG AACTTGATGG TAAGTACA (Seq. ID. No. 11)  
GTATCTATAT TCATCATAGG AAACACCATT (Seq. ID. No. 12)  
CCAGACTTCA CTTCTAATGA TGATTATGGG (Seq. ID. No. 13)  
ACATTTTCCTT TCAGGGTGTG TGAATAA (Seq. ID. No. 14)  
TTGTGGATCA AATTTTCAGTT GACTTGTCAT C (Seq. ID. No. 15)

15. (Amended) A set of primers comprising the following [diagnostic] allele specific primer and amplification primer sequences:

GTATCTATAT TCATCATAGG AAACCACA (Seq. ID. No. 16)  
GACTTCACTT CTAATGATGA TTATGGGAGA (Seq. ID. No. 17)  
TGCCATGGGG CCTGTGCAAG GAAGTATTGA (Seq. ID. No. 18)  
AGCCTATGCC TAGATAAATC GCGATAGACT (Seq. ID. No. 19)  
GTTTCACATA GTGTATGACC CTCTATATAC ACTCATT (Seq. ID. No. 20)  
CCTATGCACTAATCAAAGGA ATCATCCTGT (Seq. ID. No. 21)  
TTTGTTTATT GCTCCAAGAG AGTCATACCA (Seq. ID. No. 22)  
GCTAAAGAAA TTCTTGCTCG TTGTT (Seq. ID. No. 23)  
GACTGACTGACTGACTGACTCTGACTGACTTATTCACCTTGCTAAA  
GAAATTCTTG CTGA (Seq. ID. No. 24)  
TAAATTGGA GCAATGTTGT TTTTGACC (Seq. ID. No. 25)  
TA TTTTATT TCAGATGCCA TCTGTGAGTT (Seq. ID. No. 26)  
TTTGCTGTG AGATCTTTGA CAGTCATTT (Seq. ID. No. 27)

16. (Amended) A method according to claims 1 or 2 wherein polymerization is performed using [set of primers as claimed in any one of claims 1, 2, 3, 5, 12, 13, or 14 and comprising] one or more of the following control primers:

GAGCACAGTA CGAAAAACCA CCT (Seq. ID. No. 1)

AAACTTTTAC AGGGATGGAG AACG (Seq. ID. No. 2)

AGAGGATTAT CTATGCAAAT CCTTGTAACC (Seq. ID. No. 3)

TCAACTTCAC TATCAAAAGT CATCATCTAG (Seq. ID. No. 4).

17. (Amended) A diagnostic kit for detecting the presence or absence of twelve mutations, in the cystic fibrosis transmembrane conductor regulator (CFTR) gene which comprises sets of primers as claimed in anyone of claims [1, 2,] 3, 5, [12, 13,] 14, or 15.

Please add new claim 19 as follows:

19. (New) A set of primers as claimed in any one of claims 3, 5, or 14 and comprising one or more of the following control primers:

GAGCACAGTA CGAAAAACCA CCT (Seq. ID. No. 1)

AAACTTTTAC AGGGATGGAG AACG (Seq. ID. No. 2)

AGAGGATTAT CTATGCAAAT CCTTGTAACC (Seq. ID. No. 3)

TCAACTTCAC TATCAAAAGT CATCATCTAG (Seq. ID. No. 4).

Respectfully submitted,



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